1. (**Amended Three Times**) A method for evaluating the morphogenic activity of a candidate morphogenic protein or analog thereof, comprising:

(a) creating a local defect site in a mammal accessible to progenitor cells,

(b) administering said candidate morphogenic protein or analog systemically to said mammal at a site distal from the local defect site,

C1

(c) measuring the ability of candidate protein or analog to induce new tissue formation at said defect site, and

(d) comparing the ability of said candidate with the ability of a control to perform the same function,

wherein said local defect site is a non-neuronal defect site.

3. (**Amended Three Times**) A method for evaluating an optimal dosage of a candidate morphogenic protein or analog thereof for administering to a mammal, comprising:

(a) creating a local defect site in a mammal accessible to progenitor cells,

C2

(b) administering said candidate morphogenic protein or analog systemically to said mammal at a site distal from the local permissive defect site,

(c) measuring the ability of candidate protein or analog to induce new tissue formation at said defect site, and

(d) comparing the ability of said candidate with the ability of a control to perform the same function,

wherein said local defect site is a non-neuronal defect site.

5. (**Amended**) The method of claim 1 or 3, wherein said non-neuronal defect site occurs in skeletal, lung, cardiac, liver, pancreas, uterine, ovarian, gastrointestinal, colon, dermal, oral mucosa, osteochondral, chondral, or thyroid tissue.

C3

6. (**Amended**) The method of claim 1 or 3, wherein said non-neuronal defect site occurs in renal tissue.

7. (**Amended**) The method of claim 1 or 3, wherein said non-neuronal defect site occurs in dental or periodontal tissue.

8. (**Amended**) The method of claim 1 or 3, wherein said mammal is aged.

9. (**Amended**) The method of claim 1 or 3, wherein said mammal has a reduced capacity to induce callus formation.

10. (**Amended**) The method of claim 1 or 3, wherein said mammal is afflicted with impaired blood flow to the skeletal extremities.

11. (**Amended**) The method of claim 1 or 3, wherein said mammal has a reduced capacity to induce an endogenous morphogenetic signal.

12. (**Amended**) The method of claim 1 or 3, wherein morphogenic protein or analog is administered parenterally.

C3 cont.

13. (**Amended**) The method of claim 12, wherein morphogenic protein or analog is administered intravenously.

14. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein is administered orally.

15. (**Amended**) The method of claim 1, wherein said morphogenic protein or analog is administered to said mammal at a time when mesenchymal progenitor cells are accessible to said defect locus.

16. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein or analog is administered at least six hours after the creation of said defect.

17. (**Amended Twice**) The method of claim 1, wherein said morphogenic protein or analog is administered at least 24 hours after the creation of said defect.

18. (**Amended Twice**) The method of claim 1, wherein said morphogenic protein or analog is administered at least 72 hours after the creation of said defect.

19. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein or analog is administered to said mammal after the initiation of fibrosis at said defect locus.

20. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein or analog is administered in aqueous solution.

21. (**Amended**) The method of claim 8, wherein said mammal is a steroidal drug user.

22. (**Amended**) The method of claim 8, wherein said mammal is aged, obese, hypertensive, or afflicted with osteopenia or diabetes.

23. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen selected from: OP1, OP2, OP3, BMP2, BMP3, BMP4, BMP5, BMP6, BMP9, BMP-10, BMP-11, BMP-12, BMP-15, BMP-3b, DPP, Vg1, Vgr, 60A protein, GDF-1, GDF-3, GDF-5, GDF-6, GDF-7, GDF-8, GDF-9, GDF-10, or GDF-11.

C3 cont.

24. (**Amended Twice**) The method of claim 23, wherein said morphogen is selected from: OP1, OP2, BMP2, BMP4, BMP5, or BMP6.

25. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen comprising an amino acid sequence having at least 70% homology within the C-terminal 106 amino acids, including the conserved seven cysteine domain, of human OP1.

26. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein is OP1.

27. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein is mature OP1 solubilized in a saline solution.

28. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein comprises an amino acid sequence defined by OPX (SEQ ID No. 3); Generic Sequence 6 (SEQ ID No. 4), Generic Sequence 7 (SEQ ID No. 5); Generic Sequence 8 (SEQ ID No. 6); or Generic Sequence 9 (SEQ ID No. 7).

C3 cont.

29. (**Amended**) A method for inducing new tissue formation at a nonskeletal defect locus in a mammal, comprising administering morphogenic protein systemically to said mammal.

C4

76. (**Amended**) A method for inducing bone or cartilage formation at a defect locus in a mammal, comprising administering osteogenic protein systemically to said mammal.

The claims presented above incorporate changes as indicated by the marked-up versions below.

1. (**Amended Three Times**) A method for evaluating the morphogenic activity of a candidate morphogenic protein or analog thereof, ~~the method~~ comprising ~~the steps of~~:

(a) creating~~, for purposes of the evaluation,~~ a local defect site in a mammal accessible to progenitor cells,

(b) administering said candidate morphogenic protein or analog systemically to said mammal at a site distal from the local ~~permissive~~ defect site,

(c) measuring the ability of candidate protein or analog to induce new tissue formation at said defect site, and

(d) comparing the ability of said candidate with the ability of a control to perform the same function,

wherein said local defect site is a non-neuronal defect site.

3. (**Amended Three Times**) A method for evaluating an optimal dosage of a candidate morphogenic protein or analog thereof for administering to a mammal, ~~the method~~ comprising ~~the steps of~~:

(a) creating~~, for purposes of the evaluation,~~ a local defect site in a mammal accessible to progenitor cells,

(b) administering said candidate morphogenic protein or analog systemically to said mammal at a site distal from the local permissive defect site, ~~and~~

(c) measuring the ability of candidate protein or analog to induce new tissue formation at said defect site, and

(d) comparing the ability of said candidate with the ability of a control to perform the same function,

wherein said local defect site is a non-neuronal defect site.

5. (**Amended**) The method of claim 1 or 3, wherein said non-neuronal defect ~~locus~~ site occurs in skeletal, lung, cardiac, liver, ~~neural,~~ pancreas, uterine, ovarian, gastrointestinal, colon, dermal, oral mucosa, osteochondral, chondral, or thyroid tissue.

6. (**Amended**) The method of claim 1 or 3, wherein said ~~defect locus~~ non-neuronal defect site occurs in renal tissue.

7. (**Amended**) The method of claim 1 or 3, wherein said ~~defect locus~~ non-neuronal defect site occurs in dental or periodontal tissue.

8. (**Amended**) The method of claim 1 or 3, wherein said mammal is aged.

9. (**Amended**) The method of claim 1 or 3, wherein said mammal has a reduced capacity to induce callus formation.

10. (**Amended**) The method of claim 1 or 3, wherein said mammal is afflicted with impaired blood flow to the skeletal extremities.

11. (**Amended**) The method of claim 1 or 3, wherein said mammal has a reduced capacity to induce an endogenous morphogenetic signal.

12. (**Amended**) The method of claim 1 or 3, wherein morphogenic protein or analog is administered parenterally.

13. (**Amended**) The method of claim 12, wherein morphogenic protein or analog is administered intravenously.

14. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein is administered orally.

15. (**Amended**) The method of claim 1, wherein said morphogenic protein or analog is administered to said mammal at a time when mesenchymal progenitor cells are accessible to said defect locus.

16. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein or analog is administered at least six hours after the creation of said defect.

17. (**Amended Twice**) The method of claim 1, wherein said morphogenic protein or analog is administered at least 24 hours after the creation of said defect.

18. (**Amended Twice**) The method of claim 1, wherein said morphogenic protein or analog is administered at least 72 hours after the creation of said defect.

19. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein or analog is administered to said mammal after the initiation of fibrosis at said defect locus.

20. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein or analog is administered in aqueous solution.

21. (**Amended**) The method of claim 8, wherein said mammal is a steroidal drug user.

22. (**Amended**) The method of claim 8, wherein said mammal is aged, obese, hypertensive, or afflicted with osteopenia or diabetes.

23. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen selected from ~~the group consisting of~~: OP1, OP2, OP3, BMP2, BMP3, BMP4, BMP5, BMP6, BMP9, BMP-10, BMP-11, BMP-12, BMP-15, BMP-3b, DPP, Vg1, Vgr, 60A protein, GDF-1, GDF-3, GDF-5, GDF-6, GDF-7, GDF-8, GDF-9, GDF-10, or GDF-11.

24. (**Amended Twice**) The method of claim 23, wherein said morphogen is selected from ~~the group consisting of~~: OP1, OP2, BMP2, BMP4, BMP5, or BMP6.

25. (**Amended Twice**) The method of claim 1 or 3, wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen comprising an amino

acid sequence having at least 70% homology within the C-terminal ~~102-~~106 amino acids, including the conserved seven cysteine domain, of human OP1.

26. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein is OP1.

27. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein is mature OP1 solubilized in a saline solution.

28. (**Amended**) The method of claim 1 or 3, wherein said morphogenic protein comprises an amino acid sequence defined by OPX (~~Seq.~~ SEQ ID No. 3); Generic Sequence 6 (~~Seq.~~ SEQ ID No. 4), Generic Sequence 7 (~~Seq.~~ SEQ ID No. 5); Generic Sequence 8 (~~Seq.~~ SEQ ID No. 6); or Generic Sequence 9 (~~Seq.~~ SEQ ID No. 7).

29. (**Amended**) A method for inducing new tissue formation at a nonskeletal defect locus in a mammal, ~~the method~~ comprising ~~the step of~~ administering morphogenic protein systemically to said mammal.

76. (**Amended**) A method for inducing bone or cartilage formation at a defect locus in a mammal, ~~the method~~ comprising ~~the step of~~ administering osteogenic protein systemically to said mammal.

REMARKS

Applicants have canceled most claims directed to non-elected Groups of inventions in the parent application (claims 30-75, and 77-122) to expedite prosecution. Applicants reserve the right to prosecute claims of similar or identical scopes in future applications.

Upon entry of this amendment, claims 1, 3, 5-29, and 76 constitute pending claims in the present application. Among them, claims 1, 3, and 5-28 are under consideration in the parent application. Claims 29 and 76 are directed to non-elected inventions in the parent application. Claims 6 and 7 are directed to non-elected species of local defective sites in the parent application. Applicants note that the Examiner has acknowledged that pending claims 1, 3, and 8-22 are generic claims linking elected and non-elected species (see Paper No. 9 mailed on 11/22/00).